Trachoma elimination, approaching 2020

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Trachoma elimination, approaching 2020

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Purpose of review
To review current practices for trachoma treatment with a focus on recent studies, particularly those discussing trachoma trichiasis surgery.

Recent findings
Azithromycin eye drops twice daily for 3 days may be as efficient as oral azithromycin in treating active trachoma. Facial cleanliness and environmental improvement programming should employ a variety of behavior change techniques to give sustained improvements. Posterior lamellar tarsal rotation carries a lower risk for trichiasis recurrence and is more effective in severe trachoma trichiasis than bilamellar tarsal rotation. Tarsoconjunctival incision can play a pivotal role in trichiaisis recurrence. Tarsus-sparing procedures continue to be refined with good success rates. Concurrent correction of lid abnormalities that commonly occur with trachoma trichiasis may maximize the result of surgery.

Summary
Better understanding of the pathophysiology of trachoma and postoperative trichiasis recurrence is critical for effective trachoma control. Progressive tarsoconjunctival scarring in trachoma and high recurrence rates following tarsal rotation procedures raise the importance of adopting a procedure that spares tarsus/conjunctiva.

Keywords
anterior lamellar recession, surgery, trachoma, treatment, trichiasis

INTRODUCTION

Trachoma continues to be the leading cause of preventable blindness worldwide [1,2]. Although it has disappeared from industrialized countries, it is responsible for the visual impairment of approximately 1.9 million people, across 41 endemic countries [2].

The disease starts in early childhood with repeated *Chlamydia trachomatis* infection and recurrent episodes of chronic conjunctival inflammation. This leads to progressive conjunctival scarring causing cicatricial entropion and trichiasis [3]. Trachomatous trichiasis is probably the main risk factor for the development of blinding corneal opacification in trachoma. The WHO, through the Alliance for the Global Elimination of Trachoma (GET) by 2020, is aiming to eliminate trachoma as a public health problem by 2020. To help achieve this goal, the WHO recommends the use of the SAFE strategy: Surgery for trichiasis, Antibiotics distribution, Facial cleanliness and Environmental improvements to suppress transmission [4]. It was believed that implementation of the SAFE programme would rapidly eliminate blinding trachoma. This has only occurred in a few regions of the world [5]. As of July 2017, 10 countries have reported achieving elimination goals. Three of these countries – Mexico, Morocco and Oman – have been validated by WHO as having eliminated trachoma as a public health problem [2].

ANTIBIOTICS FOR TRACHOMA

WHO currently recommends two antibiotics for the control of trachoma; 1% tetracycline eye ointment and oral azithromycin. Tetracycline eye ointment must be used for 6 weeks. In addition to the length of treatment, ointment is difficult to apply in children and can cause blurred vision, leading to poor compliance [6,7]. Azithromycin has been the drug of choice for trachoma because of its safety in children, efficacy as a single oral dose (20 mg/kg in children or 1 g in adults) and long half-life in tissues

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KEY POINTS

- Trachoma is known to be a public health problem in 41 countries with more than 3 millions of people in need of trachoma trichiasis surgery.
- Despite the global endeavors to address the current trachoma trichiasis backlog by 2020, the high unfavorable outcome rates following tarsal rotation procedures are undermining these efforts.
- Tarsoconjunctival incision in tarsotomy procedures may speed up the progressive scarring in trachoma.
- Some studies have reported greater success with lamellar splitting followed by ALR, therefore avoiding an incision in the posterior lamella.

[8]. However, the inappropriate use of oral azithromycin is associated with bacterial resistance and systemic adverse effects in children [9–11].

A working article presented at the GET 2020 meeting discussed the advantages of azithromycin 1.5% eye drops over oral azithromycin and topical tetracycline [12]. Afghani *et al.* [13▪] have investigated the efficacy and safety of azithromycin 1.5% eye drops for treating active trachoma in children. They concluded that azithromycin eye drops twice daily for 3 days is efficient in treating active trachoma in children in endemic areas and preventing long-term ocular complications of trachoma. The studied patients were followed up for 3 years.

MASS ANTIBIOTICS DISTRIBUTION

As trachoma is a disease of entire communities, the WHO recommends mass drug administrations for 3 years in communities in which follicular trachoma is found in more than 10% of children [14]. The issue of who should be treated, how frequently, for how long and with oral or topical azithromycin is still a matter of debate.

Although the WHO standard is to treat all individuals with mass azithromycin coverage of at least 80% in the community [6,14], a recent cluster randomized trial [15] demonstrated that biannual treatment of children aged 6 months–12 years was comparable to annual treatment of the entire community which may offer lower antibiotic use and other logistical advantages. Oldenburg *et al.* [16] showed that increasing antibiotic coverage among children from 80% (the WHO recommendation) to 90% may yield only short-term improvements for trachoma control programmes.

The decision to treat for 3 years is supported by a randomized controlled trial [17] which evaluated the possibility of stopping mass distribution in low-prevalence Tanzanian communities (10–20%) if the infection rate dropped below 5% before the third round of treatment; however, the third round could not be stopped in any of the communities.

FACIAL CLEANLINESS AND ENVIRONMENTAL IMPROVEMENT

It is clear that treatment interventions should be accompanied with promotion and prevention of trachoma. If the basic hygiene factors that allowed trachoma to thrive on the site are not addressed, the disease will return once the mass distribution of antibiotics ceases [18].

Facial cleanliness and environmental improvement (F&E) programming should move beyond information dissemination, and employ a variety of behavior change techniques. A recent study showed that many F&E-related interventions do not align well with learning from the behavioral sciences. This may explain, in part, why such interventions do not yield sustained improvements in F&E behaviors and practices [19].

A Cochrane Review investigated whether face washing prevents active trachoma in endemic communities. The authors concluded that there was some evidence that face washing with topical tetracycline was beneficial, but the evidence generally did not support face washing alone or in combination with antibiotics in reducing active trachoma [20].

A child's face with no ocular and nasal discharge is considered clean and the desired endpoint. West *et al.* [21] suggested adding assessment of clean faces to trachoma surveys. Their study showed that the assessment of clean faces can be carried out reliably by different graders.

SURGERY FOR TRACHOMATOUS TRICHIASIS

Trachoma trichiasis severity spectrum

Trachoma trichiasis is a wide spectrum of disease extending from the simple to the severe forms based on the location and number of rubbing lashes and the degree of entropion [22,23]. The clinical phenotype therefore ranges from a single rubbing eyelash to the whole eyelid rolled inward [24]. Trichiasis can involve entropion, misdirected eyelashes or metaplastic eyelashes [3]. Despite the absence of obvious entropion in many trachoma trichiasis patients, the lid margin usually shows characteristic changes including rounding of the posterior border and anterior migration of the mucocutaneous junction, indicating a subtle form of entropion [3,25,26].

Who should be treated?

Although there is a broad consensus that corrective surgery is appropriate for patients with severe trachoma trichiasis, the optimal treatment for mild disease (patients with just a few, peripheral, metaplastic lashes) is uncertain. Many patients and clinicians prefer to epilate until more severe disease develops. However, attaining follow up data on unoperated patients is difficult, and progression of trachoma trichiasis can be quite rapid in some people leading to corneal opacification [18]. Therefore, WHO recommends surgery for all patients with trachoma trichiasis, irrespective of severity [24].

Which technique should be used?

Over the years, many surgical techniques have been described for trachoma trichiasis correction [26–28]. The diversity of the procedures reflects the complexity of the disease and strongly suggests that none of them offers the ultimate solution.

WHO recommends either bilamellar tarsal rotation (BLTR) or posterior lamellar tarsal rotation (PLTR) surgery for trachoma trichiasis. Both procedures entail a horizontal tarsotomy combined with everting sutures to rotate the distal portion of the lid outward [24,29]. However, a recent randomized controlled trial comparing BLTR and PLTR operations in Ethiopia showed that PLTR had a substantially lower risk of postoperative trichiasis [13% in those randomized to PLTR, and 22% in those randomized to BLTR: an absolute risk difference of 9.5% (95% confidence interval 4.8–14.2%)]. In addition, PLTR was more effective in severe trachoma trichiasis cases than BLTR [30].

Currently, there is an effort to address the current trachoma trichiasis backlog by 2020, with an increase in number of people managed for trachoma trichiasis worldwide from 139 441 (2014) to 260 759 (2016) [31]. However, high unfavorable outcome rates following surgery are undermining these efforts. Both programmatic experience and published data [24,32,33] suggest that the incidence of postoperative trichiasis recurrence is unacceptably high, occurring in 20–40% of patients by 1 year and, in one series, more than 60% of patients by 3 years after surgery [34]. In addition, a report from the Global Trachoma Mapping Project suggests the number of cases with unfavorable outcomes have increased significantly with increasing surgical output [24].

Recurrent trachoma trichiasis is probably because of various surgical and disease factors [28]. Habtamu *et al.* [35▪▪] studied the predictors of unfavorable outcomes after BLTR and PLTR. They concluded that poor postoperative outcomes in trachoma trichiasis surgery were associated with inadequate peripheral dissection, irregular incision, asymmetric suture position and tension, inadequate correction and lash location. Preoperative major trichiasis and older age were independent predictors of trichiasis recurrence for both surgical procedures.

Moreover, the progressive nature of trachomatous scarring [36] may play an important role in trichiasis recurrence. Burton *et al.* [37] found evidence of progressive scarring in cohorts of individuals from Ethiopia and Tanzania with established conjunctival scarring. In both populations, the progression was associated with conjunctival inflammation but not detectable *C. trachomatis* infection. However, the primary drivers of this late stage disease remain unclear.

It seems likely that direct tarsoconjunctival incision as in BLTR and PLTR often triggers conjunctival inflammation and further cicatrisation, which can lead to surgical failure. This is supported by findings of two trials [38,39]; one trial investigated conjunctival inflammatory cytokine and tissue remodeling responses 1 year after surgery. It was found that recurrent trichiasis was associated with a reduced the proteolytic enzyme MMP-1 to its inhibitor TIMP-1 ratio which may favor the accumulation of fibrotic tissue. A second trial showed that recurrent trachoma trichiasis was associated with increased expression of psoriasin (S100A7), before surgery and on multiple occasions with about a two-fold increase in S100A7 expression during a 2 year follow-up period. S100A7 is able to promote inflammation and may contribute to the development of the scarring process in trachoma.

These studies and the concept that tarsus involving procedures may not be the most appropriate surgery for trachoma trichiasis have led others to promote the use, or at least investigation, of tarsus-sparing procedures for the treatment of trachoma trichiasis.

Tarsus-sparing procedures

Tarsus-sparing procedures involve splitting skin and orbicularis oculi muscle from tarsus/conjunctiva and recessing/repositioning the anterior lamella with or without posterior lamella advancement [40,41]. This group of procedures has several advantages; first, the surgery is performed on structures anterior to the tarsal plate, thereby avoiding trauma to the conjunctiva [42]. Second, it preserves the integrity of the meibomian glands and theoretically avoids iatrogenic dry eye, which is particularly important in trachoma trichiasis [43].

Anterior lamellar recession

Anterior lamellar recession (ALR) is a well-known conventional surgical procedure for the correction

FIGURE 1. ALR through lid crease approach. (a) Preoperative photograph upper lid TT. (b) Evereted upper lid showing trachomatous scarring and characteristic of margin changes. (c) Excision of a skin ellipse. (d) Excision of a strip of orbicularis oculi (e) Pretarsal orbicularis muscle is raised and dissected from the tarsus, peeling the whole lid margin including the cilia. (f) The composite flap of skin and pretarsal orbicularis was recessed, sutured to anterior tarsal surface using three to four interrupted six-zero absorbable mattress sutures, leaving up to 2 mm of tarsus visible below the anterior lamella margin. (g,h) Preoperative and 6-month postoperative photographs of another patient (19-year-old female) with the cilia in good position. TT, trachoma trichiasis.

of eyelid entropion and trichiasis since first described by Welsh in 1969 [44]. It involves complete splitting of the eyelid with subsequent recession of anterior lamella several millimeters away from the lid margin. Interestingly, the procedure has many modifications and bears different names in the literature including [45]: lamellar division [42,46]; anterior lamellar reposition [47]; anterior lamellar repositioning [48]; gray line split with anterior lamellar reposition [49,50]; tarso-conjunctival advancement [51]; tarsal advance [52]; ALR; [40,53] and anterior lamellar reposition with complete lid split [43].

Anterior lamellar recession versus reposition

ALR should be differentiated from anterior lamellar repositioning that does not entail complete lamellar division. Some researchers misused the term 'anterior lamellar repositioning' for the presentation of an ALR procedure [43,47,48], whereas the technique and indications of the two procedures are not the same [42]. We advocate the use of the term ALR for procedures that involve complete lid split [40,42,53,54], whereas anterior lamellar repositioning should be reserved for those without complete splitting [42,55,56].

Anterior lamellar repositioning without complete lid split will not overcome the underlying cicatricial force at the eyelid margin because the lid margin structures are tightly bound in this area [53,57]. For the anterior lamella to be recessed on the posterior lamella without tension, complete lamellar division should be performed. This gives a potentially effective long-term result.

Eyelid crease versus gray line approach

Interlamellar separation can be performed through an eyelid crease approach [58▪▪], lid margin approach [46,47,49,56,59▪] or both [48,57]. The dissection through the upper lid crease incision only [58▪▪] and down to the lid margin can be more effective for the following reasons (Fig. 1). First, it allows for more accurate and meticulous dissection at the lid margin, the site of disease, without losing the tissue plane or inadvertently cutting through the tarsal plate which may induce further cicatrization [58▪▪]. This is especially important when the lid margin is distorted with no identifiable gray line [3,28,60]. Second, dissection can continue beyond the lash follicles, peeling the entire anterior lid margin from the tarsus in cases of metaplastic lashes and keratinization [57]. Third, it allows for addressing concurrent dermatochalasis and gives good exposure for levator surgery [43,53,58▪▪]. Finally, a lid crease approach allows for supratarsal fixation of the separated anterior lamella which helps maintain an upward vector of traction to the anterior lamella preventing its downward migration and lash eversion [53,57,58▪▪].

Gawdat *et al.* [58▪▪] described their results using eyelid crease approach for ALR without gray line incision. They addressed the concurrent lid problems including dermatochalasis, ptosis, retraction and brow ptosis through the same incision. They argued that these associated lid abnormalities can aggravate the severity of the condition and increase the risk of recurrence if not corrected simultaneously

However, Pandey *et al.* [59▪] reported a case series of upper eyelid cicatricial margin entropion with retraction, corrected through a gray-line approach only. They performed simultaneous levator recession and normal lid margin apposition was achieved in all eyes.

To cover the bare tarsus or not

The bare anterior tarsal surface during ALR can be left to epithelialize spontaneously or covered with a mucosal graft [40], amniotic membrane transplantation [43], skin graft [61] or acellular human dermal allograft [62]. Covering of the bare tarsus with different grafts is believed to act as a barrier to prevent downward migration of anterior lamella and speed healing [53]. However, no literature demonstrating this advantage over leaving bare tarsus exists.

CONCLUSION

With less than 2 years to reach 2020, the target year for elimination of blinding trachoma worldwide, there are many challenges still facing completion of the GET 2020 goals including poor surgical outcomes with high recurrence of trichiasis, the reemergence of infection after mass distribution of azithromycin in some communities and the incomplete understanding of the environmental improvements and behavioral changes. Approaches to improve and scale-up the SAFE strategy should be adopted [63].

According to the latest report of GET 2020, 3.2 million people are in need of trichiasis surgery [64]. Given the high rates of recurrent trichiasis, poor outcomes following the WHO adopted techniques and the difficult management of recurrent cases, there is an urgent need to investigate alternative techniques, particularly those sparing the tarsus, to improve surgical outcome.

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Conflicts of interest

There are no conflicts of interest.

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